



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|-------------------|
| 10/588,609 | 08/07/2006 | Hisakazu Katsuki | KATSUKI2 | 8366 |
| 1444 | 7590 | 03/20/2009 | EXAMINER | |
| BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303 | | | | QAZI, SABIHA NAIM |
| ART UNIT | | PAPER NUMBER | | |
| 1612 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 03/20/2009 | | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/588,609 | KATSUKI ET AL. | |
| | Examiner | Art Unit | |
| | Sabiha Qazi | 1612 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 08 December 2008.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 10-16 is/are pending in the application.

4a) Of the above claim(s) 16 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 10-15 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. _____.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.

5) Notice of Informal Patent Application

6) Other: _____.

Non Final Office Action

Claims 10-16 are pending. Amendments are entered. No claim is allowed. Applicants' arguments, filed 12/8/08, have been fully considered. Rejections not reiterated from previous office actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Summary of this Office Action dated 02/26/2009

1. Continued Examination Under 37 CFR 1.114
2. Information Disclosure Statement
3. Copending Applications
4. Specification
5. 35 USC § 112 (1) Written Description and New Matter Rejection
6. 35 USC § 112 (2) Rejection
7. 35 USC § 103(a) Obviousness Rejection
8. Response to Remarks
9. Communication

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/8/2008 has been entered.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within

their knowledge as to other copending United States applications, which are

"material to patentability" of the application in question. MPEP 2001.06(b).

See Dayco Products Inc. v. Total Containment Inc., 66 USPQ2d 1801 (CA FC 2003).

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 12-15 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

3. There is no description or guidance for suppressing the "generation" of isomers in the specification as has been claimed. There is no description of the "under shading" as claimed in claim 13. Applicant is kindly requested to explain this issue.

Applicant had no possession of the claimed subject matter. Specification contains no example, description, teaching or guidance so that one skilled in the art to make and use the invention as has been presently claimed.

The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to one skilled in the art that the inventor had the possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claimed language. See *In re Kaslow*, 707 F 2d 1366, 1375 (Fed. Cir. 1983).

The written description requirement prevents applications from using the amendment process to update the disclosure in their disclosures (claims or

specification) during the pendency before the patent office. Otherwise applicants could add new matter to their disclosures and date them back to their original filing date, thus defeating an accurate accounting of the priority of the invention. See 35 USC 132. The function of description requirement is to ensure that the inventor had possession, as of filing date of the application relied on, the specific subject matter claimed by him.

See *Genetech*, 108 F 3d 1361, 1365 (Fed. Cir. at 1366, 78, 1999).

Applicant is kindly requested to explain the issue.

See MPEP 2163.06

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
2. Claims 11-15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 10 and 11 are duplicate claims. There is no difference between isolated compound and the compound present in the drug.
4. What is the meaning of "generation" in claim 12?
5. It is unclear what is intended by "shading" in claim 13. The preparation is covered, away from light?
6. It is unclear what applicant mean by "standard of isomer in analysis of preparation"

35 USC § 103(a) Obviousness Rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 5-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over CHEN et al. (WO 03/047595), MIYAMOTO et al. (US Patent 4,666,634) and chem. Pharm. Bull. (all 892 references). These references teach vitamin D preparation containing ED-71, fat and oil and an antioxidant which embraces presently claimed invention. See tables, examples and claims

CHEN et al teaches pharmaceutical compositions comprising an active vitamin D compound in emulsion pre-concentrate formulations, as well as

emulsions and sub-micron droplet emulsions produced therefrom. The compositions comprise a lipophilic phase component, one or more surfactants, and an active vitamin D compound. The compositions may optionally further comprises a hydrophilic phase component. See the entire document especially [0056] where antioxidant BHA, BHT and tocopherols are taught. See [0036] and [0037] where fish oil, vegetable oils triglyceride are taught. The reference teaches active vitamin D compounds [0055] including calcitriol where antioxidants are used. The reference teaches antioxidants such as ascorbyl palmitate, butyl hydroxyl anisole (BHA), butyl hydroxyl toluene (BHT) and tocopherols and d-tocopherols (vitamin E) are taught (present specification discloses all these antioxidants). For the dosage see [0060].

CHEN does not specifically teach ED-71 or its synthesis and degradation products.

MIYOMOTO (Chem. Pharm. Bull) teaches preparation of vitamin D compounds including ED-71. Various steps and intermediates are taught. See chart 2 on page 1111, experimental section on pages 1112 and 1113 are taught.

MYOMOTO in US '634 teach synthesis of ED 71, see the entire document especially example 13 and process for preparing compound and intermediates. See columns 4-9 where intermediates and ED-71 were prepared.

Art Unit: 1612

104121-92-8 REGISTRY

ED Entered STN: 06 Sep 1986

CN 1,3-Cyclohexanediol, 2-(3-hydroxypropoxy)-4-methylene-5-[(2E)-2-[(1R,3aS,7aR)-octahydro-1-[(1R)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-

inden-4-ylidene]ethylidene]-, (1R,2R,3R,5Z)- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 9,10-Secococholesta-5,7,10(19)-triene-1,3,25-triol, 2-(3-hydroxypropoxy)-, (1 α ,2 β ,3 β ,5Z,7E)- (9CI)

OTHER NAMES:

CN 2 β -(3-Hydroxypropoxy)-1 α ,25-dihydroxyvitamin D3

CN ED 71

CN Eldecalcitol

FS STEREOSEARCH

MF C30 H50 O5

SR CA

LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS,

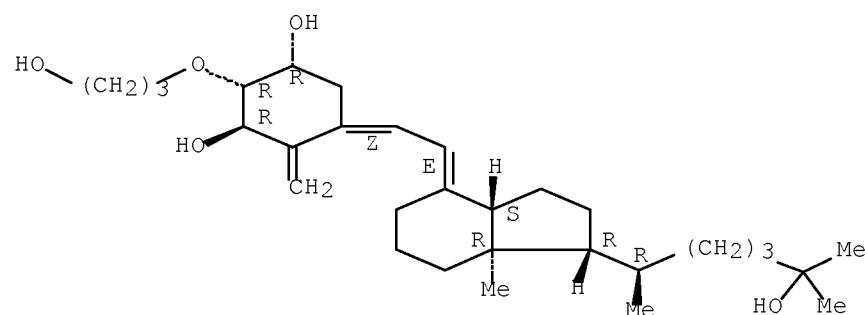
CASREACT, CHEMCATS, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS,

IMSRESEARCH, IPA, MEDLINE, PHAR, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2,

USPATFULL

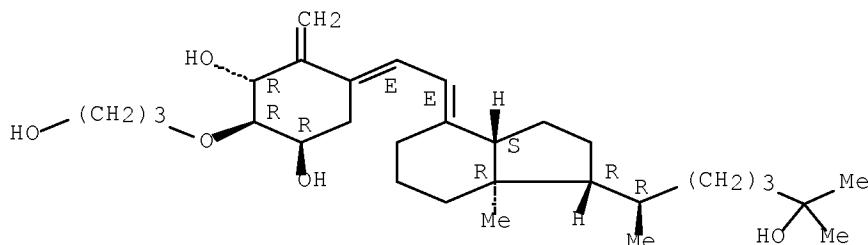
Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 861996-34-1 REGISTRY
ED Entered STN: 29 Aug 2005
CN 9,10-Secocoholosta-5,7,10(19)-triene-1,3,25-triol, 2-(3-hydroxypropoxy)-,
(1 α ,2 β ,3 β ,5E,7E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C₃₀ H₅₀ O₅
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



It would have been obvious to one skilled in the art to prepare additional beneficial preparation containing ED-71 and its intermediates or degradation products by using the ingredients, fat and oil and an antioxidant. The degradation product would be present in composition containing ED-71. Prior art does not teach the names of degradation product but the composition would inherently contain degradation products. Identification of degradation product of the known composition is not a new invention. No new concept or finding has been noted.

Motivation has been provided by the prior art to prepare composition of active vitamin D compounds such as calcitriol and ED-71. Motivation to combine the teachings of CHEN and MYOMOTO would have been obvious at the time of invention. Even in a case where the reference does not teach the same use of the composition, the two different intended uses are not distinguishable in terms of the composition, see *In re Thuau*, 57 USPQ 324; *Ex parte Douros*, 163 USPQ 667; and *In re Craige*, 89 USPQ 393.

The discovery of a new action underlying a known process does not make it patentable. *MEHL/Biophile*, 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. Also, it is irrelevant that the prior art observers did not recognize the property or function of the disputed claim; if the prior art inherently possessed that characteristic, it anticipates. See *Verdeegal Brothers, Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 633, 2 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 1987). This is believed to be applicable here because anticipation is the epitome of obviousness.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Response to Remarks

- Amended claim 11 still contains “isolated”, however, Examiner believes that the compound would have been obvious no matter it is isolated or not. After isolation compound remains the same. There will be no change in structure.
- Claim 16 is withdrawn from consideration because the subject was not examined in the previous claims. This application is an RCE and not the continuation.
- Examiner disagree that WO reference does not teach “antioxidants”. Examiner respectfully disagrees because the reference teaches ascorbyl palmitate, butyl hydroxyl anisole (BHA), butyl hydroxyl toluene (BHT) and tocopherols and d-tocopherols (vitamin E) are taught. Present specification discloses all these antioxidants.
- Applicant argue that trans ED-71 is more active than ED-71 in differentiation. However, there is no mention in the specification that this compound is useful other than synthesis. “The ED-71 preparation of the present invention makes it possible to provide a pharmaceutical formulation capable of suppressing the generation of a degradation product of ED-71. The trans form of ED-71 is useful as a standard in the analysis of ED-71 preparation and is also useful as a material for the synthesis of various types

of vitamin D- based compounds". See paragraph [0095]. Furthermore the abstract of the invention as disclosed in the publication on STN further supports examiners point that the trans compounds is the degradation product and Applicants are trying to suppress the formation of this compound. The publish abstract (DN 143:199944, CAPLUS, abstract of WO 200574943) is "Disclosed is a pharmaceutical preparation which can inhibit (5Z,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)- triene-1,3,25-triol (ED-71) from yielding tachysterol and the trans isomer, which are major products of the decomposition of ED-71 during storage at room temperature. The pharmaceutical preparation comprises (5Z,7E)-(1R,2R,3R)-2-(3- hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol, a fat, and an antioxidant. For example, a composition containing ED-71, ethanol 1.3, dibutylhydroxytoluene (BHT) 0.02, and medium-chain triglyceride balance to 100 % was filled in a gelatin soft capsule shell". Claim 13 of the present invention is drawn to 1R,2R)-1,25-dihydroxy-2-(3'-hydroxypropoxy)-cholecalciferol; 2.beta.-(3'-hydroxypropoxy)-(1.alpha.,3.beta.,5Z,7E)-9,10-secocholesta-5,7 ,10(19)-triene-1,3,25-triol (ED-71).

]0092] As can be seen from Table 8, all the antioxidants used remarkably suppressed the generation of the **tachysterol** and trans forms. [0093]

Example 5: (page 34), **dl-a-tocopherol** (manufactured by Wako Pure Chemical Industries, Ltd.), **dibutylhydroxytoluene** (manufactured by Wako Pure Chemical Industries, Ltd.), **butylhydroxyanisole** (manufactured by Wako Pure Chemical Industries, Ltd.),

Furthermore the arguments is that trans is better than ED-71, however examiner notes that preparation as claimed are not drawn to trans ED-71.

The trans ED-71 is a degradation product and is present in ED-71 in a very small quantity. The preparation taught by WO reference contains all the ingredients as claimed. Nothing new was found in the preparation of ED-71.

Preparation of trans isomer of ED-71 was not disclosed and was not intended in the disclosure. It is a degradation produce of ED-71.

ADVANTAGE OF THE INVENTION as disclosed in present specification

[0019] The ED-71 preparation of the present invention makes it possible to provide a pharmaceutical formulation capable of suppressing the generation of a degradation product of ED-71. The trans form of ED-71 can be used both as a

standard in the analysis of an ED-71 preparation and as a material for the synthesis of various types of vitamin D- based compounds.

Applicant further argue that new claim 13 specifies that (SE, TE)-(IR, 2R, 3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25- triol (trans form of ED-71) is an isolated compound. Examiner believes that the chemical structure of the compound is the same no matter it has been isolated or synthesized.

The data presented in the declaration has been fully considered. The data shows trans to be more active than ED-71. However, claim 1 and its dependent claims are not drawn to trans ED-71.

See KSR Supreme Court of United States Decision KSR INTERNATIONAL CO. v. TELEFLEX INC. et al. No. 04-1350; 550 U.S.-, 82 USPQ 2d 1385 (2007) where it states that (1) "However, the issue is not whether a person skilled in the art had the motivation to combine the electronic control with an adjustable pedal assembly, but whether a person skilled in the art had the motivation to attach the electronic control to the support bracket of pedal assembly". (2) "the results of ordinary innovation are not the subject of exclusive rights under the patent laws". In the present case the as claimed would have been obvious to one skilled in the art at the time the invention was made.

CONCLUSION

In summary Examiner concludes that claims and specification does not provide any new concept, improvements for the reasons cited above. To emphasize this point Examiner would like to refer Applicants to Genetech, 108 F.3d at 1366 and Brenner 383 U.S. 519, 536, 148 USPQ 689, 696 (1966)" which states that "a patent is not a hunting license. It is not a reward for research, but a compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague limitations of general ideas that may or may not be workable."

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day except Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sabiha Qazi/
Primary Examiner, Art Unit 1612

Application/Control Number: 10/588,609
Art Unit: 1612

Page 20